URETERITIS CYSTICA CHRONICA.*

REPORT OF A CASE WITH BILATERAL DOUBLE URETERS.

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THE object of this short paper is to review the conclusions reached on this subject by well-known authorities, and particularly to invite consideration to some recent experimental work by Dr. R. Giani, of Turin, Italy, which throws considerable light on this much-debated pathological problem.

The subject is one that has proven thus far solely of pathological interest, although the writer sees no reason why under certain conditions a skilled cystoscopist should not detect this condition during life.

Morgagni,[1] Rayer,[2] and Rokitansky[3] were the earliest writers to mention this affection, the latter describing the same in the following clear, concise manner:

"In the mucous membrane of the urinary tract, especially of either ureter, generally in large numbers and groups, there sometimes arise cysts varying in size from that of a grain of wheat to that of a pea, and others of microscopical dimensions. They contain a thin serous or thick colloid, clear or yellowish brown fluid, or gluey resinous clumps."

Virchow[4] maintained that these cysts are true retention cysts, the same as the ordinary mucoid cysts of the vagina, and are caused by a closure of the crypts of the mucous glands of the bladder and ureter.

Litten[5] was the first to give a careful microscopical study of these cysts, and concludes without reservation that the inflammatory catarrh of the mucous membranes of the ureters led to a closure of its crypts and glands, retaining within their lumen their secretions, thus leading to a cystic formation.

Why these cysts occur so rarely in comparison to the

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great frequency of inflammation and catarrh of these mucous membranes he explains on the ground of the very wide openings of these crypts and the scarcity and uncertain distribution of the glands in these mucous membranes.

R. v. Limbeck,[6] as early as 1887, gives an accurate description of this disease and its etiology as judged in the light of Giani's experiments, to be explained later on. He mentions two ways whereby these cysts take their origin:

First, through a union of folds of the proliferating mucous membrane; and second, by a budding process of its epithelium with later a central degeneration and liquefaction of these newly formed epithelial nests and sprouts.

That glands might possibly occur in these mucous membranes and thus by closure of their exits become a source of these cysts he does not deny, but he states that he with many others has failed to find any such glands.

The English writers, Silcock,[7] Eve,[8] Clarke,[9] Bland-Sutton,[10] have accurately described cases of this affection and have drawn particular attention to certain peculiar round or ovoid bodies that are constantly found within the cystic contents, which bodies they interpreted as forms of sporozoa.

Clarke claimed to have found bodies with large nuclei, a well-marked network, and a nucleolus; conditions only compatible with a perfect state of vitality of cell life. He believed there was an appearance as though the cell was in the process of mitosis, although he failed to discover any mitotic figures. He thought it highly improbable that such bodies arose from degenerated epithelium and strongly maintained that they were some variety of protozoa and the direct cause of this disease.

Prof. G. Pisenti [11] describes a case of cystic pyelonephritis, the right ureter containing numerous irregularly distributed cysts, and the left likewise, though fewer in number. The neck of the bladder also possessed numerous thickly placed small cysts whose contents were a clear fluid. In these various cysts he found the same bodies interpreted by the English writers as protozoa, and he coincides with them as regards their etiological importance. He offers no proof that he ever discovered

any signs of life in these bodies or that by experiment he was able to reproduce the disease through their agency. His conclusions are simply based upon microscopical observations, whereby, claiming not to have found within these cysts any transition forms of epithelium, he concludes that these peculiar bodies must be of parasitical and not cellular origin.

V. Kahlden,[12] in an exhaustive monograph on this subject, also concludes that in his case the histogenesis rests upon a parasitic basis, although he does not definitely attempt to classify these supposed parasites, but simply states it as his belief, because of the great similarity between the bodies he found within these cysts and the myxosporidia (a psorosperm found in the bladders of fishes, particularly the pike), that therefore they are either a variety of this class of sporozoa or identical with them. He produces no evidence to support his conclusions from artificial cultivation of these parasites, nor from the reproduction of this disease through their agency by inoculation of lower animals.

One fact opposing the parasitic origin of this disease and prominently claiming our attention is, that no one as yet has found any of these protozoa in or among the epithelial cells of the mucous membrane of the genito-urinary tract or even the cells lining the walls of these cysts. They always appear in the colloidal mass within the cysts. It certainly seems reasonable to expect to find them occasionally (if only by accident) in or among the cellular epithelium when they are present in such large numbers and are supposed to be the causative factor in the formation of these cysts out of the epithelium of the mucous membrane of this tract.

A. v. Brunn's[13] studies on the normal mucous membrane of the genito-urinary tract have proven of great service in elucidating this problem, by showing the existence of certain epithelial bodies found beneath the superficial layer of cells of the mucous membrane, either disconnected therefrom or in direct continuance with the same. He claims that they are in no sense secretory glands, as was formerly held by Virchow and Litten, since they fail to show a constant exit duct or

central lumen, which is generally present in most glandular structures, and that there is never present within these cells any of those changes frequently observed in glandular organs while functionating. He believes these cellular accumulations are the result of a simple budding process of the normal mucous membrane, due to an excessive stimulation and consequent proliferation of the surface epithelium. When these bodies are not disconnected from the surface he speaks of them as epithelial buds or sprouts, and the others, disconnected by an intervening layer of connective tissue, as epithelial cell nests. It is from these cellular formations, he maintains, that the condition of cystitis and ureteritis cystica chronica arises.

Lubarsch[14] strongly contends against the parasitic origin of these cysts and agrees with v. Brunn, as he has observed all stages of degenerative transition of these epithelial cell nests from solid to complete cystic formations. Clear and forceful is the conclusion to be drawn therefrom, that this is the true origin of these cysts, the two things necessary being the presence of v. Brunn's cell nests and the continuous action of some injurious agent, the most frequent being inflammation arising from the existing calculi. The cysts arise by, first, a destruction of the centrally located cells, out of which later is formed a colloid and granular detritus. Since this material finds no exit, by its increment the cyst increases in size until there is but a single layer of epithelial cells that bound the lumen of the ureter. He concludes from microscopical examination and the peculiar action of stains on these cell contents that the same is not a true secretion, but simply a colloid mass originating from degenerated epithelium.

Lubarsch by no means thought that this was the sole method of origin of these cysts, for at the close of his article he really speaks of three ways: namely, those cysts that arise from the closure of mucous crypts as described by Virchow and Litten, those that come from a degeneration of v. Brunn's cell nests, and those that are found at the trigone of the bladder, due to misplaced prostatic glandular tissues.

Aschoff's[15] extensive studies on the mucous membrane of the genito-urinary tract would go to prove that in the newly born and those of early life no epithelial budding of the mucous membrane or cut-off epithelial nests, as described by v. Brunn and Lubarsch, can be found in the genito-urinary tracts, and even in adult life he found them to be very inconstant and chiefly confined to the upper third of the ureter.

Marckwald[16] found cystitis and ureteritis cystica in the newly born, and claims, as does Aschoff, that an inflammation is not first necessary to originate these cell nests and cysts.

Stoerk,[17] on the other hand, after a most painstaking and exhaustive study of this subject, differs from v. Brunn in that he claims these cell buds and nests are secretory in nature as well as their contents, and that it is by the retention of their secretions that a transformation of these gland-like cell nests into cysts occurs.

He also differs from the views of Aschoff and Marckwald in that he strongly maintains that there must be first an inflammatory reaction to cause these cell nests, even though traces of such a reaction may have entirely disappeared from present view. He draws attention to one very significant fact that certainly requires explanation, which is, that during extra-uterine life nowhere in the body in any of the other mucous membranes can any analogy to v. Brunn's findings be discovered. What explanation can be offered that the mucous membrane of the genito-urinary tract solely and frequently undergoes this proliferating budding process?

Giani,[18] in a purely accidental way, was surprised to find a condition simulating in every respect cystitis and ureteritis cystica chronica caused by some experiments he had instituted for a study of tuberculosis of the genito-urinary tract. He performed a suprapubic cystotomy upon rabbits, and placed within the bladder some gelatin capsules containing a pure culture of tubercle bacilli. The external wound and bladder healed regularly. Free passage of urine occurred a few hours after the operation. In one case about 30 days later the capsule was passed through the urethra. In all the other cases the

capsules became the seat of salty incrustations from the urine, and were the centres of well-formed and quite large calculi. The rabbits, twelve in all, were kept alive from fourteen days to three months. After fifteen days he discovered a chronic cystitis, and scattered here and there in numerous places the mucous membrane showed marked tendency toward proliferation of its epithelial cells in more or less bud-like processes dipping down into the stratum proprium. Later these became wholly separate from the mucous membrane. Still later he found degeneration and liquefaction taking place within their centres, and thus the beginning of a small cyst. These epithelial submucous nests varied very materially in size. Sometimes they remained throughout one solid mass of epithelial cells. Complete cystic formation rarely occurred before the fortieth day, from which time on they increased considerably in size and number. He universally found these cysts, in toto or in part, filled with a fine granular detritus composed of red blood corpuscles, leucocytes, fragments of nuclei, and broken-down epithelial cells. Besides these, he frequently found in these cystic contents peculiar bodies, whose form was generally round or elliptical, averaging in size about 20 to 25 micra, though sometimes they were as large as 40 and some were as small as 7 or 8. The protoplasm of these bodies possessed no particular structure. It was more or less coarsely granular and refractory against aniline dyes, having a hyaline, almost glassy, appearance, coloring intensely with eosin. Sometimes they contained no nucleus, then again he found a body simulating a nucleus, which stained deeply with hematein.

This description corresponds very closely to that of the so-called parasites (protozoa) supposed to have been found in the cysts by certain English and Italian writers and claimed by them to be their cause. Such bodies were found only in the cysts and never free in the epithelium of the mucous membrane, nor in the solid cell nests above spoken of and out of which cysts eventually arose, nor in the cell accumulations on the surface of the mucous membrane.

In the light of these experimental findings it is not possi-

ble further to give credence to the parasitic origin of this affection. The chronic irritation due to the inflammation set up by the capsules that acted as foreign bodies seems an essential etiological factor.

Giani found the cysts greatest in number where the irritation would appear to have been the greatest.

Further experimentation by ablation of the mucous membrane of the bladder by a Volkmann sharp spoon produced similar results.

Giani also observed in the case of hypertrophy of the prostate where the middle lobe was removed by suprapubic cystotomy that the mucous membrane of the bladder over this lobe was covered by numerous epithelial indentations and epithelial nest formations in the submucosa, either isolated or in direct communication with the surface epithelium. These undoubtedly arose from chronic irritation of the mucous membrane of the bladder at this part, due both to the hypertrophic middle lobe of the prostate and the daily repeated catheterizations which had taken place for the past three years.

In conclusion one question appears difficult to answer, and I cannot help but believe that there is still a very important factor in the etiology of this disease that is yet to be explained.

Ureteritis cystica chronica is a very rare affection. Lubarsch in over 3000 autopsies met the condition but four times. The writer's experience, which certainly covers many hundreds of autopsies, has met with the condition but once; the specimen shown in figure 1. I find in the entire literature not over 50 cases reported.

If we are to believe that inflammatory irritations of mucous membrane of the genito-urinary tract set up a proliferation of its epithelial surface so that buds and cell nests are formed, out of which later cysts are formed, then why, knowing as we do that inflammation of this tract is of very frequent occurrence, is cystitis and ureteritis cystica chronica so rarely met with? There are several cases reported in the literature of double ureter on one side in which this affection was found.

The specimen which is the basis of the present communication is one of bilateral double ureters in which there is complete cystic degeneration of all four ureters. So far as I have been able to glean from the literature, it remains the only specimen of its kind. The cystic degeneration in this case is confined to the ureters. Why?

Is the presence of ureteritis cystica in these cases of reduplication of the ureter purely a concomitant circumstance, or has the congenital malformation some etiological significance?

I am not able to answer these seemingly pertinent questions.

Microscopical examination of many sections showed all the finding of the authors above reported, especially the round and ovoid bodies in the cyst contents, the budding sprouts and cell nests in the mucous membrane of the ureters with degenerated cell and detritus material in their centres. Nothing was observed that would appear to enhance further the microscopical findings already reported, illustrations of which are plentiful in the literature herewith appended, nor to throw new light on the etiology of this much-vexed problem.

Clinical History.—Anna Palil, 40, Hungarian, houseworker. Admitted to Metropolitan Hospital, New York, May 17, 1906. Died, May 22, 1906, 9.25 A.M.

Family history negative. Does not use alcohol. Moderate tea and coffee drinker. No drug habits. Had usual diseases of childhood. Had an attack of articular rheumatism in adult life. No history of any venereal diseases. For the past three years has been complaining of her stomach. Refuses solid food. Says same causes her much distress. No history of any vomiting. No localized pain anywhere in body. Poorly nourished. Subcutaneous and muscular tissues wasted. Œdema of both lower extremities. Abdomen presents a large ventral hernia. Face has a pained and distressed appearance. Complexion is generally sallow with some cyanosis. Mucous membranes congested. No œdema of face. Reflexes are all normal. Apex beat in sixth interspace and slightly to the left of the mid-clavicular line. Border of dullness to the right reaches the mid-sternal line. Slight

K. L., the two sides of the bladder after bisection; A. B., two ureters on left side; E. F., two ureters on right side; C.D., opening of ureter into bladder.

epigastric pulsation. A rough systolic murmur is heard at the apex, the same being transmitted to the left axilla. The second pulmonic sound is accentuated. The chest expansion is poor and appears slightly greater on the left side than the right. The apices are somewhat sunken. The interspaces are very much retracted and the ribs correspondingly prominent. Over the entire chest is heard a broncho-vesicular respiration except a small area anteriorly on the right side corresponding to about the location of the right middle lobe and the base of the left lung where no respiratory murmur is heard. Large inspiratory moist rales heard over the entire lungs. Expectorates a thick muco-purulent sputum. No tubercle bacilli. Examination of abdominal organs proved negative. Urinalysis showed: light amber color, 1.028 specific gravity, albumin, no sugar, and 1 per cent of urea. Amount was 24 ounces in 24 hours.

Diagnosis.—Mitral insufficiency with failing compensation, chronic bronchitis and œdema of the lungs, chronic Bright's disease.

Autopsy.—Autopsy demonstrated the presence of chronic bronchitis, passive congestion and œdema of the lungs. Unresolved pneumonia of the middle lobe of the right lung. Chronic pleurisy. Hypertrophy and advanced fatty degeneration of the heart muscle with acute endocarditis of the mitral valve. Muscular insufficiency of the mitral and tricuspid valves. Cyanotic induration of the spleen. Early stage of cirrhosis of the liver. Chronic atonic gastritis. Passive congestion of the intestines. Chronic cystitis. Ascending pyelonephritis with hydronephrosis and advanced arteriosclerotic granular nephritis. Complete bilateral reduplication of both ureters. Extensive ureteritis cystica chronica of all four ureters. The bladder contained a foul, stinking, greenish fluid. Its walls were intensely congested. The ureters and pelves of both kidneys likewise contained a foul, stinking, greenish-yellow pus.

There is a reduplication of the ureter on both sides. Each of the four ureters arises from a separate pelvis of the kidney. The two ureters on each side remain entirely separate and distinct throughout (being divided by ordinary connective tissue and unite in one common exit at the usual normal ureteral opening at the trigone of the bladder. (See illustration.)

Each of the four ureters is very thickly studded from origin

to within 4 cm. of their exit into the bladder by innumerable cysts varying in size from that of a millet seed to that of an ordinary pea.

These cysts are both individual and massed in groups. Some are transparent and contain a clear serous fluid. Others are of an opaque greyish-yellow color containing a thick ropy colloid material. A few seem harder than the others and contain a gluey resinous-like hard substance.

The pelves of both kidneys contain likewise a few scattered similar cysts whereas the bladder is entirely free from cysts of any kind. The right kidney is very firm in consistence, of a dark mahogany brown color and weighs 62½ grams. It measures 8 by 5 by 3 cm. It is coarsely granular on its external surface and the same is studded with numerous small individual and grouped abscesses.

Its capsule is thickened and cannot be removed without adhering kidney tissue. The cut surface is granular. The cortex ranges from 1 to 3 mm. The pelves are intensely congested and inflamed. The one pelvis is in direct communication with three large well defined abscess cavities that extend to within 1 mm. of the external surface of the kidney.

The pyramids are greatly distorted or entirely replaced by tough connective tissue. The blood vessels are prominent and arteriosclerotic. The left kidney weighs 93½ grams and measures 8½ by 4 by 3½ cm. Its color consistency and other characteristics are very similar to those of the right kidney. Within the kidney and in direct communication with the pelvis of the kidney are large well defined abscess cavities that contain a foul, stinking, greenish-yellow pus.

LITERATURE.

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